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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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EXAMINER	
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ART UNIT	PAPER NUMBER
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DATE MAILED:  
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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

## Office Action Summary

Application No. <b>08/973,303</b>	Applicant(s) <b>Dormer</b>	
Examiner <b>Karen Canella</b>	Art Unit <b>1642</b>	

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 months MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

1)  Responsive to communication(s) filed on \_\_\_\_\_

2a)  This action is FINAL.      2b)  This action is non-final.

3)  Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle* 1035 C.D. 11; 453 O.G. 213.

### Disposition of Claims

4)  Claim(s) 36-39, 41, 42, 45-67, and 69-72 is/are pending in the applica

4a) Of the above, claim(s) 48-61 and 63-65 is/are withdrawn from considera

5)  Claim(s) \_\_\_\_\_ is/are allowed.

6)  Claim(s) 36-39, 41, 42, 45-47, 62, 66, 67, and 69-72 is/are rejected.

7)  Claim(s) \_\_\_\_\_ is/are objected to.

8)  Claims \_\_\_\_\_ are subject to restriction and/or election requirem

### Application Papers

9)  The specification is objected to by the Examiner.

10)  The drawing(s) filed on \_\_\_\_\_ is/are objected to by the Examiner.

11)  The proposed drawing correction filed on \_\_\_\_\_ is: a)  approved b)  disapproved.

12)  The oath or declaration is objected to by the Examiner.

### Priority under 35 U.S.C. § 119

13)  Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a)  All b)  Some\* c)  None of:

1.  Certified copies of the priority documents have been received.

2.  Certified copies of the priority documents have been received in Application No. \_\_\_\_\_

3.  Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\*See the attached detailed Office action for a list of the certified copies not received.

14)  Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

### Attachment(s)

15)  Notice of References Cited (PTO-892)

18)  Interview Summary (PTO-413) Paper No(s) \_\_\_\_\_

16)  Notice of Draftsperson's Patent Drawing Review (PTO-948)

19)  Notice of Informal Patent Application (PTO-152)

17)  Information Disclosure Statement(s) (PTO-1449) Paper No(s) \_\_\_\_\_

20)  Other

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### **DETAILED ACTION**

1. Please note that the examiner assigned to your application has changed.
2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.
3. After review and reconsideration, the finality of the rejection of 9/01/99 has been withdrawn.
4. Claims 36-38 have been amended. Claims 71 and 72 have been added. Claims 48-61 and 63-65, drawn to non-elected inventions, remain withdrawn from consideration. Claims 36-39, 41, 42, 45-47, 62, 66, 67 and 69-72 are under consideration.

#### *New Grounds of Rejection*

5. Claims 36-39, 41, 42, 45-47, 62, 66, 67 and 69-72 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 36 and 72 recite “optionally with an expression of the corresponding mRNA...”. Optionally, does not clearly describe the claimed subject matter since it cannot be determined if the claims include the limitations following the word “optionally”.

Claims 41 and 47 recite, “ a partial amino acid sequence encoded by the DNA hybridizing to the cDNA”. It is unclear if this partial amino acid sequence is completely encoded by the hybridizing DNA or if the hybridizing DNA consists of a fragment of the coding sequence.

6. The amendment filed 6/11/98 is objected to under 35 U.S.C. 132 because it introduces new matter into the disclosure. 35 U.S.C. 132 states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows: Claim 70 is drawn to a protein encoded by nucleotides 74-154 or 155-685. The disclosure as originally filed does not teach these specific nucleotide fragments.

Applicant is required to cancel the new matter in the reply to this Office action.

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7. 35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

8. Claims 36-39, 41, 42, 45-47, 62, 66, 67 and 69-72 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific, substantial asserted utility or a well established utility. The instant claims are drawn to an isolated protein having inducing differentiation of murine erythroleukemia cell line transformed by the Friend virus. The specification teaches that the differentiation is measured by hemoglobin formation in the Friend cell line. The specification also teaches that the human leukemia cell line, K562, also exhibits hemoglobin formation when contacted with the claimed isolated protein. However, the specification fails to provide any objective evidence that the claimed protein can differentiate untransformed human leukemia cells ex vivo. It is well known in the art that Friends cells are virally transformed and therefore, replicate and differentiate in a manner dependent on the presence of the virus (Ebert et al, Cancer Research, 1976, Vol. 36, pp. 18091813) Clearly, it cannot be anticipated that the claimed proteins would induce hemoglobin formation in primary leukemia cells taken from patients not infected or transformed by virus. Further, the specification fails to provide any teachings regarding the maturity of the differentiated leukemia cells, and it is well known in the art that although many agents can induce hemoglobin formation in Friend leukemia cells, the treated cells do not complete the maturation process, in that they do not extrude their nuclei and form mature erythrocytes (Tsiftsoglou et al, PNAS, 1979, Vol. 76, pp. 6381-6385) and there are no teachings in the specification regarding how to use erythroid cells which have not extruded nuclei to become erythrocytes. The specification essentially gives an invitation to experiment wherein the artisan is invited to elaborate a functional use for the disclosed protein. Because the claimed invention is not supported by a specific, substantial asserted utility for the reasons set forth, credibility of any utility cannot be assessed.

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9. Claims 36-39, 41, 42, 45-47, 62, 66, 67 and 69-72 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

10. In the event that Applicants might be able to overcome the 35 USC 101 rejection above, the specification would still be enabling only for claims limited to polynucleotides that encode SEQ ID NO:3 and 5, degenerate coding sequences thereof and the polynucleotides comprising SEQ ID NO:1, 2, 4 and 6-10 and the complete complements of said polynucleotides, because the specification does not reasonably provide enablement for polynucleotides that encode fragments of SEQ ID NO:3 and 5, amino acid fragments of SEQ ID NO:3 and 5, or polynucleotide variants or fragments of SEQ ID NO:1, 2, 4 and 6-10. The specification does not enable any person skilled in the art to which it pertains or with which it is most nearly connected, to make/use the invention commensurate in scope with these claims. Claims 41 and 67 are drawn to a protein comprising a fragment encoded by a DNA which hybridizes to SEQ ID NO:1, 2, 4. Claims 42 and 62 are drawn to protein variants of the claimed differentiation inducing factor. Claim 47 is drawn to proteins which comprise fragments of the claimed differentiation inducing factor. Claim 66 is drawn to fusion proteins comprising fragments of the claimed differentiation inducing factor. However, the specification has not taught how to make proteins comprising fragments of the disclosed differentiation inducing factor that retain the function of the original SEQ ID NO:3 or 5 and further, the specification has not shown that polynucleotides encoding polypeptide variants of the disclosed differentiation inducing factor are capable of functioning as that which is suggested. Clearly as the specification does not enable the claims for the use of SEQ ID NO:1-10 for the reasons given in paragraphs 8 and 9 above, it does not enable claims drawn to polynucleotide or polypeptide variants or fragments. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with the claims since the specification gives no guidance on or

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exemplification of how to make the polynucleotides that encode the broadly claimed polypeptides. Protein chemistry is probably one of the most unpredictable areas of biotechnology. For example, as disclosed by Burgess et al. (Journal of Cell Biology, 1990, Vol. 111, pp. 2129-2138), replacement of a single lysine reside at position 118 of acidic fibroblast growth factor by glutamic acid led to the substantial loss of heparin binding, receptor binding and biological activity of the protein. In transforming growth factor alpha, replacement of aspartic acid at position 47 with alanine or asparagine did not affect biological activity while replacement with serine or glutamic acid sharply reduced the biological activity of the mitogen ( Lazar et al, Molecular and Cellular Biology , 1988, Vol. 8, pp.1247-1252). These references demonstrate that even a single amino acid substitution or what appears to be an inconsequential chemical modification will often dramatically affect the biological activity and characteristic of a protein. Clearly, it could not be predicted that polynucleotide, or a variant, that encodes a protein or protein comprising a fragment of SEQ ID NO:3 or 5 would function as suggested. Reasonable correlation must exist between the scope of the claims and scope of enablement set forth, and it cannot be predicted from the disclosure how to make polynucleotides encoding fragments or variants of the disclosed differentiation inducing factor comprising SEQ ID NO:3 and 5, or polypeptides comprising fragments of SEQ ID NO:3 and 5 that will function as SEQ ID NO:3 and 5. In view of the above, one of skill in the art would be forced into undue experimentation to practice the claimed invention.

*Claim Rejections - 35 USC § 102*

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

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12. Claims 36-39, 45-46, 66 and 69-72 rejected under 35 U.S.C. 102(b) as being anticipated by Dormer et al (Experimental Hematology, 1992, Vol. 20, p. 758). The instant claims are drawn to an isolated protein having differentiation-inducing activity on Friend erythroleukemia cell lines comprising properties of hemoglobin formation, molecular weight range, mRNA expression pattern, cDNA and mRNA encoding said protein. Dormer et al discloses an isolated protein produced by WEHI-3B cells, said protein inducing globin mRNA transcription and subsequent differentiation in F4N and B8/3 Friend erythroleukemia cell lines. Dormer et al does not disclose specific molecular weight range, mRNA expression pattern, cDNA and mRNA encoding said protein, however, these limitations represent inherent properties of the differentiation-inducing activity.

### *Conclusion*

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen Canella whose telephone number is (703) 308-8362. The examiner can normally be reached on Monday through Friday from 8:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, can be reached on (703) 308-3995. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Karen A. Canella, Ph.D.  
Patent Examiner, Group 1642  
July 29, 2001

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KAREN A. CAPUTA  
PRIMARY PATENT EXAMINER  
COMPUTER TECHNOLOGY CENTER 1600